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(54) Title: T CELL BINDING LIGAND PEPTIDES, PEPTIDE CONSTRUCTS CONTAINING SAME AND USE THEREOF FOR TREATMENT OF IMMUNOLOGICAL DISORDERS

(57) Abstract:

Title: T Cell Binding Ligand Peptides, Peptide Constructs Containing Same and Use Thereof For Treatment of Immunological Disorders

(1) Field of the Invention

This invention relates to peptide constructs useful in modulating the immune system of humans and other mammals, and to a peptide useful as a T cell binding ligand (TCBL) for directing a CD4 related T helper cell response, when the TCBL is linked to a disease associated antigenic peptide to form the peptide conjugate. More particularly, this invention relates to a derivative of Peptide G (the fifteen-mer peptide sequence from MHC IIβ chain (135-149), previously used as a T cell binding ligand for forming immunogenic peptide constructs, and which derivative enhances the immune response of immunogenic peptide constructs as compared to the same peptide conjugates but in which the non-derivatized Peptide G is used. In particular, this invention relates to an immunogenic composition useful to activate the immune system of a patient exposed to or at risk of infection by human immunodeficiency virus (HIV-1) which is the causative organism of the disease known as Acquired Immune Deficiency Syndrome (AIDS). This invention also relates to other peptide constructs for treating other specific immunological disorders and diseases and to the methods for treating individual subjects to modify the subjects immune system response.

(2) Discussion of the Prior Art

One of the present inventors has previously discovered a class of immunologically active and diagnostic peptide constructs obtained by joining one or more T cell binding ligands with an antigenic peptide. These peptide constructs are described in, for example, U.S. 5,652,342, the entire disclosure of which is incorporated herein, in its entirety, by reference thereto. These peptide constructs have been referred to by the assignee of the aforementioned patent by the trademark, L.E.A.P.S.™, an acronym for the coined expression, "Ligand Epitope Antigen Presentation System." More recently, specific classes of peptide constructs, based on the L.E.A.P.S. technology, have been developed for a number of specific immunological disorders, including, for example, HIV-1 (e.g., SN 08/695,304,), HSV (e.g., PCT/US98/20681), autoimmune disease (e.g., SN 60/161,734), the disclosures of which are incorporated herein in their entireties.

As described in these prior patent documents, linking of a T cell binding ligand to a peptide epitope could alter the nature of the immune response (i.e., cell mediated (TH1) - CD4 related TH1 or antibody (TH2)). It was further shown that the antibodies derived from certain conjugated peptides were better able to recognize the native molecule than were the antibodies prepared using a conventional peptide-KLH conjugate. It was shown that antibodies induced by the conjugated peptide (also referred to as "peptide construct") had a broader specificity, so that they

recognized the peptide epitope not only in the free linear peptide form, but also in the native molecule. In some cases, the use of the peptide conjugated to KLH was not able to recognize the epitope in the native molecule.

As exemplary of the T cell binding ligand portion of the above described peptide constructs, a portion of the MHC Class II β from residues 135-149 (Peptide G) was used and achieved good results. The long range stability of the peptide constructs formed using Peptide G, was carried out with the construct dissolved in saline (0.15 M NaCl, pH 7.4) or in water for injection (WFI) at a concentration of 0.5-2.0 mg/ml and stored frozen soon after preparation. It was noticed (using HPLC methods applied to the above construct solutions maintained at temperatures of 2-8°C, i.e., refrigerated; or 18-25°C, i.e., room temperature; or 40°C, i.e., elevated, over periods of hours to days, and at pH values of from 7.4 down to 4.5) that the peptide constructs are prone to a deamination reaction, especially prevalent at more alkaline (higher) pH's. The deamination was observed at the amino terminus and yielded either an isoaspartic or aspartic acid residue at the N terminus.

Accordingly, further improvements in the long term stabilization of the conjugated peptides are desirable to enhance the value of these immunomodulators. In addition, new peptide constructs based on this modified TCBL and other TCBLs, for modulating the immune system of individual subject are desired.

SUMMARY OF THE INVENTION

The present invention is based, in part, on the discovery that a modified version of Peptide G (Asn Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile - SEQ ID NO:2) obtained by replacing Asn with Asp to form Peptide G' (Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile - SEQ ID NO:1) overcomes the long range stabilization problem of the peptide conjugates and, quite surprisingly, also enhances the immune response, particularly the CD4 related (cell mediated) response, of conjugated peptides (L.E.A.P.S. constructs) as previously described.

Accordingly, in one aspect, the present invention provides a novel peptide having SEQ ID NO:1, useful as a TCBL in forming conjugated peptides having immunological activity by directing a host to mount a Th1 response to an antigenic peptide present in the peptide construct.

According to another aspect, the present invention also provides conjugated peptide constructs obtained by covalently bonding the peptide having SEQ ID NO:1, directly, or preferably via a divalent linking group, to an antigenic peptide.

In accordance with still another aspect of the invention, there is provided a pharmacologically effective composition obtained from the above mentioned peptide construct and a pharmaceutically acceptable carrier.

In yet another aspect of the invention, there are provided new peptide constructs obtained by linking Peptide J (Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu - SEQ ID NO:34) to various antigenic Cancer Muc1 peptides, CEA peptides, and others, and useful to modulate the immune response of individual subjects in need thereof.

This invention also provides a method for treating a patient suffering from an immunological disorder by administering to the patient a therapeutically effective amount of a peptide construct in which a peptide having SEQ ID NO:1 or SEQ ID NO:34 is covalently bonded to an antigenic peptide associated with the immunological disorder.

In accordance with a specific embodiment, the present invention relates to a peptide construct comprising a first T cell specific binding peptide having SEQ ID NO:1 and a second peptide covalently linked together, wherein the second peptide is an antigenic peptide of from about 25 to about 37 amino acids (which is referred to hereinafter as "modified HGP-30") and which is capable of eliciting preferentially TH1 associated antibodies when administered to a human in need thereof. The antigenic or second peptide has sequence identity (including naturally occurring variants and alleles thereof) with the p17 gag protein of HIV-1 wherein the peptide has a sequence originating with an amino acid residue chosen from residues 76 to 83 and ending with an amino acid residue chosen from residues 107 to 112 of p17 gag

protein of HIV-1. In particular, the second or antigenic peptides disclosed in the aforementioned copending application SN 08/695,304, or copending application SN 08/695,301, the disclosures of which are incorporated herein in their entirety by reference thereto.

Peptide G', used as T cell specific binding molecule in the conjugated peptides of this invention will bind specifically or at least preferentially to specific class or subclass of T cells, such as helper T cells, T_h, suppressor T cells, T_s, cytotoxic T cells, CTL, and the like.

The second or antigenic peptide used to form the peptide construct of this invention, may be any known or subsequently discovered antigenic peptide, including, for example, any of the antigenic peptides mentioned in any of the above patents or copending patent applications, including, without limitation, peptides associated with herpes simplex virus (HSV), malaria, tuberculosis, cancers, AIDS, allergies, autoimmune diseases, such as, arthritis, Graves disease, multiple sclerosis (MS), myocarditis, diabetes, Lupus, and the like.

In accordance with a preferred aspect of the invention, the antigenic peptide is a portion of p17 of human immunodeficiency virus (HIV-1) and, particularly, a peptide of from about 25 to 37 amino acids, extending in the range from residues 76 to 112, such as the amino acid sequences shown by the following representative cases:

A T L Y S V H Q R I D V K D T
K E A L E K I E E E (SEQ ID NO:3)

S L Y N T V A T L Y S V H Q R
I D V K D T K E A L E K I E E
E Q N K S K (SEQ ID NO:4)

R S L Y N T V A T L Y S V H Q
R I D V K D T K E A L E K I E
E E Q N K S K (SEQ ID NO:5)

In any of these sequences of modified HGP-30, it will be understood that one or more additional amino acids in the sequence from residues 76 to 112 may be added at either the N- or C- terminal, and similarly, one or more amino acids may be deleted from either terminal, while maintaining the total length from about 25 to about 37 amino acids.

A particularly preferred antigenic peptide for use in this invention has the following amino acid sequence

A T L Y S V H Q R I D V K D T
K E A L E K I E E E Q N K S (SEQ ID NO:6)

SEQ ID NO:6, (sometimes referred to, for convenience, as m-HGP-30, or even more simply as "mH"), representing a modified version of HGP-30 (see, e.g., U.S. 4,983,387).

While the following discussion will focus primarily on the conjugated peptides containing the sequence of Peptide G' and the sequence for a modified HGP-30, it is to be understood that other antigenic peptides, whether from HIV-1, HIV-2, or other disease causing organism, or antigenic peptide associated with a particular disease, disorder or condition, may be used in place of modified HGP-30 with expectation of similar results.

The conjugated peptides formed from Peptide G' and a modified HGP-30 offer the advantages previously seen with other conjugated peptides, such as those more generally disclosed in the aforementioned U.S. 5,652,342, of inducing broad spectrum antibodies but, additionally providing a desired TH1 specificity believed to result from the second or antigenic peptide which incorporates a CTL epitope which may modify the response to the desired isotype.

The present invention also relates to pharmaceutically effective compositions containing such antigen-peptide G' constructs (for convenience, may sometimes be referred to as "heteroconjugate") for eliciting immunization to infection against Human Immunodeficiency Virus, HIV-1, in a human subject. Such compositions, in addition to the heteroconjugate of this invention will, preferably, include suitable immunological adjuvant(s).

Similarly, the invention relates to the use of such heteroconjugate and the pharmaceutically effective composition containing same for treating or preventing HIV-1 infection and Acquired Immunodeficiency Complex (AIDS) by administering to a human patient in need thereof, a therapeutically or prophylactively effective amount of the heterofunctional conjugate as defined above.

DETAILED DESCRIPTION OF THE INVENTION AND PREFERRED EMBODIMENTS

For the peptides disclosed in this application, the amino acid sequences thereof, are set forth by the single letter and three-letter identification symbols as follows:

Amino Acid	Three-letter abbreviation	One-letter symbol
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asn	N
Aspartic Acid	Asp	D
Cysteine	Cys	C
Glutamine	Gln	Q
Glutamic Acid	Glu	E
Glycine	Gly	G
Histidine	His	H
Isoleucine	Ile	I
Leucine	Leu	L
Lysine	Lys	K

Methionine	Met	M
Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V

In particular, in accordance with one specific embodiment of the invention, pertaining to peptide constructs useful for improving the immune system of individuals exposed to, infected by, or at risk for exposure to the AIDS virus, the antigenic peptides useful in this invention will generally be between about 25 and 37 amino acids, as represented in the following exemplary cases including examples of a longer and shorter antigenic peptides:

A T L Y S V H Q R I D V K D T
K E A L E K I E E E (SEQ ID NO:3)

S L Y N T V A T L Y S V H Q R
I D V K D T K E A L E K I E E
E Q N K S K (SEQ ID NO:4)

R S L Y N T V A T L Y S V H Q
R I D V K D T K E A L E K I E
E E Q N K S K (SEQ ID NO:5)

m-HGP-30 (mH) having the following sequence is especially preferred:

Ala Thr Leu Tyr Ser Val His Gln Arg Ile Asp Val Lys Asp Thr Lys Glu Ala Leu Glu Lys Ile Glu Glu Glu Gln Asn Lys Ser

or, using the corresponding single letter identifiers:

ATL YSV HQR IDV KDT KEA LEK IEE EQN KS (SEQ ID NO:6)

It should be understood that in any of the above amino acid sequences of antigenic peptides, variations of specific amino acids which do not adversely effect the desired biological activity are contemplated and included within the scope of the invention. In particular, it is recognized that the foregoing sequences are based upon a specific variant of HIV-1, namely, HIV-1 SF2 (actually, the Ser^{86} analog of the natural Cys^{86} sequence) and, although this region of interest of HIV-1 is generally fairly highly conserved, other naturally occurring and spontaneously occurring variants, including from one or several (e.g., up to about 10) variations of the amino acids are within the sequences of interest. Such natural and spontaneously occurring amino acid variations are specifically contemplated and, in certain cases, it may be advantageous to use mixtures of peptides, the sequences of which, may, correspond to two or more natural and spontaneously occurring variants of HIV-1.

Still further, as well recognized in the art, it is often advantageous to make specific amino acid substitutions in order, for example, to provide specific binding sites or for purpose of introducing a label, e.g., radioactive or fluorescent tagging, of the peptide. Such "designed" amino acid sequences are also within the scope of the antigenic peptides (e.g., modified HGP-30) of this invention.

Examples of different consensus sequences of HIV-1 which are also specifically included within the scope of the modified HGP-30 antigenic peptides for use as the second peptide in the conjugated peptides of this invention include, for instance, the following, taken from "HIV-1 Sequence Database, Human Retroviruses and AIDS 1996: A Compilation and Analysis of Nucleic Acid and Amino Acid Sequences", edited by G. Myers, et al., Theoretical Biology and Biophysics Group, Los Alamos National Laboratory, Los Alamos, NM, December 1996, and any of the subsequent yearly updates thereof. The lower case letters represent potential or known cites of amino acid variability resulting from the allelic variations, genetic drift and mutations of the particular consensus sequence; the presence of a "?" symbol reflects that there was, at the time of publication, no agreed upon consensus for the amino acid at that position of the consensus sequence:

CONSENSUS A:

kSL fNt vat Lyc vHq rId

vkD tKe Ald kiE eiq nKs k SEQ ID NO:7

CONSENSUS B:

rSL yNt vat Lyc vHq rIe

vkD tKe Ald kiE eEq nKs k SEQ ID NO:8

CONSENSUS C:

rSL ?Nt vat LyC vH? ?Ie

vrD tKe Ald kiE eEq nK? Q SEQ ID NO:9

CONSENSUS D:

kSL ?Nt vat Lyc vHe rIe

vkD tKe Ale kmE eEq nKs k SEQ ID NO:10

CONSENSUS F:

rSL yNt vav Lyf vHq rvE

vkD tKe Ald KLE eEq nKs q SEQ ID NO:11

CONSENSUS G:

kSL ?N? ?a? L?c ?Hq rIe

vkD tKe Ale EVE Kaq kns Q SEQ ID NO:12

CONSENSUS H:

QSL fNL La? Lyc vHq rId

?kD tKe Al? k?? e?q n?? Q SEQ ID NO:13

CONSENSUS O:

?SL WNA I?V LWc vHN r??

I?D tQQ AIQ kLK eVM ?sR K SEQ ID NO:14

A "most likely" sequence over the region of interest, transcending the different subtypes is also given in the 1996 publication, as follows:

KSL FNT VAV LYC VHQ RIE VKD TKE ALD K.. ... . SEQ ID NO: 15

Sequences of, and identification of, specific species within each of these subtypes are available in the published literature, including not only the 1996 Myers, et al, publication, *supra*, but also, other annual Los Alamos Compendia, including Human Retroviruses and AIDS 1999: A Compilation and Analysis of Nucleic Acid and Amino Acid Sequences, CL Kuiken, et al, Eds., Theoretical Biology and Biophysics Group, Los Alamos National Laboratory, Los Alamos, New Mexico, 1999. These databases, such as, "HIV-1 Sequence Database, 1998/1999 HIV-1 and SIV alignments," are available on the Internet at web site (URL): http://hiv-web.lanl.gov which includes a link to: http://hiv-web.lanl.gov/ALIGN_CURRENT/00get_align.cgi, the latter including sequences for many different subtypes of HIV-1, the disclosure of which is incorporated herein by reference thereto, and a copy of which is appended to this application.

Any of these or other naturally occurring species within Consensus A, Consensus B, Consensus C, Consensus D, as well as Consensus F, Consensus G, Consensus H, Consensus O, whether presently known or existing, or subsequently discovered or subsequently arising, can be used as the modified HGP-30

antigenic peptide in the peptide constructs of this invention. It is well known in the art that these various consensus sequences are generally derived from, and are prevalent in different geographical regions of the world and are often referred to as "clades" (also known as "subtypes") of the HIV-1 virus.

Representative of these clades of modified HGP-30 include the following consensus sequences (wherein the letter designations generally correspond to the consensus sequences as given above) and any allelic variations thereof:

Thailand-B:

YCV HQK IEV KDT KEA LEK IEE EQN KSK KKA SEQ ID NO:16

Thailand-A/E:

WCV HQR IEV KDT KEA LDK IEE VQN KSQ QKT SEQ ID NO:17

Uganda-A:

YCV HQR IDV KDT KEA LNK IEE MQN KNK QRT SEQ ID NO:18

Kenya-A:

YCV HQR IDV KDT KEA LDK IEE IQN KSK QKT SEQ ID NO:19

Brazil-A/E:

YFV HQR VEV KDT KEA LDK LEE EQN KSQ QKT SEQ ID NO:20

Brazil-B:

YCV HQK IDV RDT KEA LEK VEE EQN KSK EKA SEQ ID NO:21

Uganda-B:

YCV HQR IDV KDT KEA LDK IEE EQN KSK KKE SEQ ID NO:22

Uganda-C:

YCV HKG IEV RDT KEA LDK IEE EQN KIQ QKT SEQ ID NO:23

India-C:

YCV H?? IEV RDT KEA LDK IEE EQN K?Q QKT SEQ ID NO:24

Uganda-D:

YCV HER IKV ADT KEA LDK IEE EQT KSK KKA SEQ ID NO:25

As can be seen from the above aligned consensus sequences and species for the various consensus sequences, there is some variation amongst HIV-1 subtypes in the gag protein sequence. Moreover, there is considerable variation in the specific numbering of amino acids among different HIV-1 strains. In the present invention, the numbering of sequences is based on the sequence of clade B HIV-1 strain SF2 or MN (most recently revised to MNCG); however, it is the amino acid sequence itself, allowing for variations observed amongst HIV-1 subtypes, that is important. The sequences as described above and in the appended literature are illustrative of the types of amino acid changes that can be made in the antigenic modified HGP-30 peptides of the invention and the conjugated peptides based thereon.

In particular HIV-1 SF2 (Clade B) has the following sequence in the region from residue 76 to residue 112:

RSL YNT VAT LYC VHQ RID VKD TKE ALE KIE EEK QKS K

SEQ ID NO:26

while HIV-1 MNCG (Clade B) has the following sequence in the region from residue 76 to residue 112:

KSL YNT VAT LYC VHQ KIE IKD TKE ALE KIE EEQ NKS K

SEQ ID NO:27

In addition to the variations in the amino acids among the various HIV-1 strains, it is also recognized that the amino acids at the N-terminal and C-terminal may be present as the free acid (amino or carboxyl groups) or as the salts, esters, ethers, or amides thereof. In particular amide end groups at the C-terminal and acetylation, e.g., myristyl, etc. at the N- or C-terminal, are often useful without effecting the immunological properties of the peptide.

The conjugated peptides and the constituent components thereof can be prepared by conventional processes for synthesizing proteins, such as, for example, solid phase peptide synthesis, as described by Merrifield, R. B., 1963, J. of Am. Chem. Soc., 85:2149-2154. It is also within the scope of the invention and within the skill in the art to produce the novel peptide constructs of this invention or the peptide components thereof by genetic engineering technology.

In the present invention, the above modified HGP-30 antigenic peptides are covalently linked to Peptide G'.

Peptide constructs prepared by linking the antigenic peptides based on the modified HGP-30 epitopes to Peptide G' have been shown by the inventors to elicit an immune response to HIV-1 that can be directed toward the desired TH1 response as evidenced by the numerous examples of the TH1 characteristic antibody IgG2a (mouse) or IgG3 (man) induction. The order of Peptide G' and

second modified HGP-30 peptide is not usually critical and may be reversed. For example, if modified HGP-30 (B) is linked to G' then the peptide construct may have the sequence G'-B or B-G'. Also, while Peptide G' and modified HGP-30 may be directly coupled to each other, it is preferred that a small linker sequence or a larger heterolinker molecule may be used to couple the two peptides. For example, as the spacer, one or a few, up to about 5, preferably, up to about 3 or 4, neutral amino acids, such as glycine, may be used to link the peptides. Preferred spacer peptides include, for example, GGG, and GGGGS, however, the spacer may be made larger or smaller and altered to include other molecules or amino acids, besides the amino acid glycine, such as in GGGGS. Examples of other known spacers which may be used for covalently linking two or more peptides or proteins or equivalent DNA sequences, include, for example, GGGSGGGS (SEQ ID NO:93); GGGGSGGGGSGGGGS (SEQ ID NO:94); GGGGSS (SEQ ID NO:28); GGGGSGGGGSGG (SEQ ID NO:29); GGGSGTGSGSGS (SEQ ID NO:30); GGGGSGGGSGGGS (SEQ ID NO:31); KGKGKGL (SEQ ID NO:32) and VAKLEAKVAKLEAKGKGKY (SEQ ID NO:33).

As examples of heterolinkers mention may be made of, for example, N-succinimidyl-3-(2-pyridylthio)propionate (SPDP), m-maleimidobenzoyl-N-hydroxy-succimide (MBS) as well as any of the other reagents employed to link peptides, including without limitation those disclosed in the aforementioned US 5,652,342.

The administration of the peptide constructs of this invention may be carried out alone or in conjunction with other therapy. Examples of other therapies which may be used in conjunction with the peptide constructs of this invention include, in the case of treatments (prophylactic or therapeutic) for infection by HIV-1, for example, protease inhibitors, reverse transcriptase inhibitors, zinc binding inhibitors, and the like.

The peptide constructs of this invention, may be represented by formula (I):

Peptide G'-x-P* (I)

wherein Peptide G' is the peptide having SEQ ID NO:1

x is a direct bond or divalent linking group; and

P* is an antigenic peptide associated with AIDS, especially HIV-1.

The conjugated peptides of formula (I) may be used to direct the immune response prophylactically (e.g., to a CD4 directed immune response) to prevent infection or reduce the likelihood of infection by HIV-1, or to direct the immune response therapeutically (e.g., to a TH1 directed immune response) in HIV-1 infected individuals, perhaps in conjunction with other therapies, to reduce viral load and to control or cure the infection by HIV-1. The peptide constructs may also be used to direct the immune response prophylactically to induce a TH1 (cellular), TH2 (antibody) or mixed TH1/TH2 directed immune response to prevent or reduce the infection by HIV-1, or to

direct the immune response therapeutically to induce a TH1, e.g., $CD4^+$, TH2 or mixed TH1/TH2 directed immune response against the AIDS virus, perhaps in conjunction with other therapies to reduce the viral load and to control or cure the infection by HIV-1 in HIV-1 infected subjects.

The peptide constructs of this invention may be used as a component of an immunomodulatory composition, together with one or more pharmaceutically acceptable carriers or adjuvants, either prophylactically or therapeutically. When provided for use prophylactically, the immunomodulatory composition is provided in advance of any evidence of infection by HIV-1. The prophylactic administration of the composition should serve to prevent or attenuate HIV-1 in mammals. In a preferred embodiment a human, at high risk for HIV-1 is prophylactically treated with the peptide conjugate of this invention, as such, or as a component of an immunomodulatory composition. When provided therapeutically, the peptide construct or composition containing same is provided to enhance the HIV-1 infected patient's own immune response to the HIV-1 antigen.

The peptide construct is, in the case of treatments for individuals exposed to the AIDS virus, preferably administered after disease symptoms and viral load have been reduced or stabilized by Highly Active AntiRetroviral therapy (HAART).

While it is possible for the immunogenic peptide construct to be administered in a pure or substantially pure form, it is preferable to present it as a pharmaceutical composition, formulation or preparation.

The formulations of the present invention, both for clinical and for human use, comprise a conjugated peptide as described above, together with one or more pharmaceutically acceptable carriers and, optionally, other therapeutic ingredients, especially therapeutic immunological adjuvants. The carrier(s) must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not deleterious to the recipient thereof. The formulations may conveniently be presented in unit dosage form and may be prepared by any method well-known in the pharmaceutical art.

In general, the formulations are prepared by uniformly and intimately bringing into association the active ingredient with liquid carriers or finely divided solid carriers or both, and then, if necessary, bringing the product into the desired formulation.

Formulations suitable for intravenous, intramuscular, subcutaneous, or intraperitoneal administration conveniently comprise sterile aqueous solutions of the active ingredient(s) with solutions which are preferably isotonic with the blood of the recipient. Such formulations may be conveniently prepared by dissolving solid active ingredient in water containing

physiologically compatible substances such as sodium chloride (e.g. 0.1-2.0M), glycine, and the like, and having a buffered pH compatible with physiological conditions to produce an aqueous solution, and rendering the solution sterile. These may be present in unit or multi-dose containers, for example, sealed ampoules or vials.

The formulations of the present invention may incorporate a stabilizer or excipient. Illustrative excipients include polyethylene glycol, glycerol, proteins, saccharides, amino acids, inorganic acids, and organic acids which may be used either on their own or as admixtures. These excipients, when used, are preferably incorporated in an amount of about 0.1 to about 10,000 parts by weight per part by weight of immunogen. If two or more stabilizers are to be used, their total amount is preferably within the range specified above. These excipients are used in aqueous solutions at the appropriate concentration and pH. The specific osmotic pressure of such aqueous solutions is generally in the range of about 0.1 to about 3.0 osmoles, preferably in the range of about 0.8 to about 1.2. The pH of the aqueous solution is adjusted to be within the range of about 5.0 to about 9.0, preferably within the range of 6-8. In formulating the immunogenic conjugated peptide of the present invention, anti-adsorption agent may be used.

Additional pharmaceutical methods may be employed to control the duration of action. Controlled release preparations may be achieved through the use of polymer to complex or absorb the conjugated peptide. The controlled delivery may be exercised by selecting appropriate macromolecules (for example polyester, polyamino acids, polyvinyl, pyrrolidone, ethylenevinylacetate, methylcellulose, carboxymethylcellulose, or protamine sulfate) and the concentration of macromolecules as well as the methods of incorporation in order to control release.

Another possible method to control the duration of action by controlled-release preparations is to incorporate the conjugated peptide into particles of a polymeric material such as polyesters, polyamino acids, hydrogels, poly(lactic acid) or ethylene vinylacetate copolymers.

Alternatively, instead of incorporating these agents into polymeric particles, it is possible to entrap these materials in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization, for example, hydroxy-methylcellulose or gelatin-microcapsules and poly(methylmethacrylate) microcapsules, respectively, or in colloidal drug delivery systems, for example, liposomes, albumin microspheres, microemulsions, nanoparticles, and nanocapsules or in macroemulsions.

When oral preparations are desired, the compositions may be combined with typical carriers, such as lactose, sucrose, starch, talc, magnesium stearate, crystalline cellulose, methyl cellulose, carboxymethyl cellulose, glycerin, sodium alginate or gum arabic among others.

The peptide constructs of the present invention may be supplied in the form of a kit, alone, or in the form of a pharmaceutical composition as described above.

Administration of the peptide constructs and immunomodulatory compositions containing same can be conducted by conventional methods. For example, the immunogenic peptide construct can be used in a suitable diluent such as saline or water, or complete or incomplete adjuvants. The immunogen can be administered by any route appropriate for immune system stimulation, such as intravenous, intraperitoneal, intramuscular, subcutaneous, nasal, oral, rectal, vaginal, and the like. The immunogen may be administered once or at periodic intervals until, for example, a significant titer of $CD4^+$ or $CD8^+$ T cell and/or antibodies directed against the HIV-1 antigen is obtained. In particular, the antigenic peptide constructs of the invention elicit TH1 associated antibodies and other aspects of a TH1 immune response. The presence of such cells may be assessed by measuring cytokine secretion specific for TH-1 (e.g., IFN-γ,

IL-2) or TH-2 (e.g., IL-4, IL-10) in response to being pulsed with the immunogen. The antibody may be detected in the serum using conventional immunoassays.

As noted above, the administration of the peptide constructs of the present invention and the immunomodulatory compositions containing same may be for either a prophylactic or therapeutic purpose. When provided prophylactically, the immunogen is provided in advance of any evidence or in advance of any symptom due to HIV-1, or other disease causing organism, especially in patients at significant risk for occurrence. The prophylactic administration of the immunogen serves to prevent or attenuate HIV-1, or other disease or condition associated with the antigenic peptide component of the conjugated peptide in a human or other animal. When provided therapeutically, the immunogen is provided at (or after) the onset of the disease or at the onset of any symptom of the disease. The therapeutic administration of the immunogen serves to attenuate the disease.

The invention also concerns a method for treating or preventing human acquired immunodeficiency syndrome (AIDS) caused by infection with HIV-1, by administering to a human patient in need thereof a therapeutically effective amount of the peptide construct of this invention, such as the peptide construct of formula (I), wherein the antigenic peptide P* is an antigen associated with AIDS, especially, one of the antigenic peptides from p17, as previously described.

Similarly, for treatment of other disease, condition or disorder, the antigenic peptide P*, will be chosen from the antigenic peptides associated with or causing the particular disease, disorder or condition, such as previously described, for example, in U.S. 5,652,342, or any of the other copending applications described above, or any other of the myriad known antigenic peptides associated with disease or causing disease.

In this regard, peptide constructs of the following formula (II) are also provided by the present invention:

$$P^1\text{-}x\text{-}P^2 \qquad \text{(II)}$$

where P^1 represents the peptide having SEQ ID NO:1 or SEQ ID NO:34;

x represents a direct bond or divalent linking group; and

P^2 represents a peptide associated with disease, including immunological disorders, autoimmune diseases, and conditions;

As non-limiting examples of other antigenic peptides represented by P^2 mention may be made of, for example,

antigenic peptides associated with autoimmune myocarditis, such as Peptide My: DSA FDV LSF TAE EKA GVY K (SEQ ID NO:42);

antigenic peptides associated with cancer, especially Muc1, such as M1a, having the sequence APD TRP AP (SEQ ID NO:43); M1b, having the sequence STA PPA HGV (SEQ ID NO:44); M1c, having the sequence GVT SAP DTR PAP GST APP AH (SEQ ID NO:45);

CEA antigenic peptides, such as, for example:

C1: YSL GAN LNL (SEQ ID NO:46)

C2: EAQ NTT YL (SEQ ID NO:47)

C3: QYS WFV NGT F (SEQ ID NO:48)

C4: TYA CFV SNL (SEQ ID NO:49)

C5: IYP NAS LLI (SEQ ID NO:50);

antigenic peptides associated with Herpes Simplex Virus, such as, for example,

$gD1_{8-23}$: SLK MAD PNR FRG KDL P (SEQ ID NO:51)

$gD1_{1-23}$: KYA LAD ASL KMA DPN RFR GKD LP (SEQ ID NO:52);

extgB1: ERI KTT SSI EFA RLQ FTT DHI Q (SEQ ID NO:53);

antigenic peptides associated with HIV-1, including not only those previously described, but also those associated with p24, GP41, GP120, or GP160.

The divalent linking group x may be a direct bond or any of the divalent linking groups or spacers as previously described.

As examples of peptide constructs according to formula (II), mention is made of the following representative examples:

DGQ EEK AGV VST GLI GGG APD TRP AP (SEQ ID NO:54)

DGQ EEK AGV VST GLI GGG STA PPA HGV (SEQ ID NO:55)

DGQ EEK AGV VST GLI GGG GVT SAP DTR PAP GST APP AH (SEQ ID NO:56)

DGQ EEK AGV VST GLI GGG YLS GAN LNL (SEQ ID NO:57)

DGQ EEK AGV VST GLI GGG EAQ NTT YL (SEQ ID NO:58)

DGQ EEK AGV VST GLI GGG QYS WFV NGT F (SEQ ID NO:59)

DGQ EEK AGV VST GLI GGG TYA CFV SNL (SEQ ID NO:60)

DGQ EEK AGV VST GLI GGG IYP NAS LLI (SEQ ID NO:61)

DLL KNG ERI EKV EGG GAP DTR PAP (SEQ ID NO:62)

DLL KNG ERI EKV EGG GST APP AHG V (SEQ ID NO:63)

DLL KNG ERI EKV EGG GG VTS APD TRP
APG STA PPA H (SEQ ID NO:64)

DLL KNG ERI EKV EGG GYL SGA NLN L (SEQ ID NO:65)

DLL KNG ERI EKV EGG GEA QNT TYL (SEQ ID NO:66)

DLL KNG ERI EKV EGG GQY SWF VNG TF (SEQ ID NO:67)

DLL KNG ERI EKV EGG GTY ACF VSN L (SEQ ID NO:68)

DLL KNG ERI EKV EGG GIY PNA SLL I (SEQ ID NO:69)

DGQ EEK AGV VST GLI GGG KYA LAD ASL
KMA DPN RFR GKD LP (SEQ ID NO:70)

DLL KNG ERI EKV EGG GKY LAD ASL
KMA DPN RFR GKD LP (SEQ ID NO:71)

DGQ EEK AGV VST GLI GGG SLK MAD PNR
FRG KDL P (SEQ ID NO:72)

DLL KNG ERI EKV EGG GSL KMA DPN RFR
GKD LP (SEQ ID NO:73)

DLL KNG ERI EKV EGG GLY RTF AGN PRA
GGG KYA LAD ASL KMA DPN RFR GKD LP (SEQ ID NO:74)

DLL KNG ERI EKV EGG GER IKT TSS IEF ARL
QFT TDH IQ (SEQ ID NO:75)

DGQ EEK AGV VST GLI GGG ERI KTT SSI EFA
RLQ FTT DHI Q (SEQ ID NO:76)

DLL KNG ERI EKV EGG GAT LYS VHQ RID VKD
TKE ALE KIE EQN KS (SEQ ID NO:77)

DLL KNG ERI EKV EGG GSG GGS ATL YSV HQR
IDV KDT KEA LEK IEE EQN KS (SEQ ID NO:78)

DLL KNG ERI EKV EGG GGS GGG GSG GGG SAT
LYS VHQ RID VKD TKE ALE KIE EEQ NKS (SEQ ID NO:79)

DLL KNG ERI EKV EGG GGS SAT LYS VHQ
RID VKD TKE ALE KIE EEQ NKS (SEQ ID NO:80)

DGQ EEK AGV VST GLI GGG ATL YSV HQR IDV
KDT KEA LEK IEE EQN KS (SEQ ID NO:81)

DGQ EEK AGV VST GLI GGG SGG GSA TLY SVH
QRI DVK DTK EAL EKI EEE QNK S (SEQ ID NO:82)

DGQ EEK AGV VST GLI GGG GSG GGG SGG GGS
ATL YSV HQR IDV KDT KEA LEK IEE EQN KS (SEQ ID NO:83)

DGQ EEK AGV VST GLI GGG GSS ATL YSV HQR
IDV KDT KEA LEK IEE EQN KS (SEQ ID NO:84)

DLL KNG ERI EKV EGG GSL YNT VAT LYS VHQ
RID VKD TKE ALE KIE EEQ NKS (SEQ ID NO:85)

DLL KNG ERI EKV EGG GSG GGS SLY NTV ATL
YSV HQR IDV KDT KEA LEK IEE EQN KS (SEQ ID NO:86)

DLL KNG ERI EKV EGG GGS GGG GSG GGG SSL
YNT VAT LYS VHQ RID VKD TKE ALE KIE
EEQ NKS (SEQ ID NO:87)

DLL KNG ERI EKV EGG GGS SSL YNT VAT LYS
VHQ RID VKD TKE ALE KIE EEQ NKS (SEQ ID NO:88)

DGQ EEK AGV VST GLI GGG SLY NTV ATL YSV HQR IDV KDT KEA LEK IEE EQN KS (SEQ ID NO:89)

DGQ EEK AGV VST GLI GGG SGG GSS LYN TVA TLY SVH QRI DVK DTK EAL EKI EEE QNK S (SEQ ID NO:90)

DGQ EEK AGV VST GLI GGG GSG GGG SGG GGS SLY NTV ATL YSV HQR IDV KDT KEA LEK IEE EQN KS (SEQ ID NO:91)

DGQ EEK AGV VST GLI GGG GSS SLY NTV ATL YSV HQR IDV KDT KEA LEK IEE EQN KS (SEQ ID NO:92)

According to this invention the immune response induced by the conjugated peptide is at least predominantly directed toward at least the desired TH1 response as evidenced by the TH1 characteristic antibody IgG2a (mouse) and presumably thereby IgG3 (man). These peptide conjugates may, however, in addition to a TH1 elicited immune response, elicit a TH2 immune response, and in particular, a mixed TH1/TH2 immune response.

Accordingly, the antigenic peptide constructs of this invention provide potentially powerful vaccines for preventing infection by, or treating cells infected by, HSV and many other infectious and viral diseases or other immunogenic disorders and conditions. Therefore, the present invention provides such vaccine compositions which can be used to immunize patients at risk for, or exposed to the causative organism associated with a particular disease or disorder, such as, HSV, and various forms of cancer.

The present invention, therefore, provides antigenic peptide constructs, which provide powerful vaccines for neutralizing and/or killing infected cells. Therefore, the vaccines of this invention can be used to immunize patients at risk for or exposed to various diseases (e.g., bacterial or viral caused diseases, e.g., herpes simplex virus, tuberculosis, diabetes, and the like) as well as other immunological disorders caused by exposure to an antigen, including, for example, allergies, asthma, autoimmune diseases, such as myocarditis, and the like.

When used as a vaccine in the method of this invention, the vaccine can be introduced into the host most conveniently by injection, intramuscularly, intradermally, parenterally, orally or subcutaneously. Any of the common liquid or solid vehicles may be employed, which are acceptable to the host and which do not have any adverse side effects on the host or any detrimental effects on the vaccine. Phosphate buffered saline (PBS), at physiological pH, e.g. pH 6.8 to 7.2, preferably pH 7, may be used as a carrier, alone or with a suitable adjuvant. The concentration of immunogenic peptide construct may vary from about 0.5 to 200 μg/kg, such as about 25 μg/kg per injection, in a volume of clinical medium (e.g., solvent) generally from about 0.1 to 1 ml, such as about 0.2 ml, preclinical studies in animals, and from about 0.5 ml to about 2 ml, such as about 1 ml in humans. Multiple injections may be required after the initial

injections and may be given at intervals of from about 2 to 8 weeks, or other suitable time interval, for example, about 2 weeks in animals and about 8 weeks in humans, when multiple injections are given.

A preferred concentration of immunogenic peptide construct in the vaccines of the present invention may be in the range of from 10 to 25 μg/kg, however, a higher or lower dose may be administered as needed.

Example 1

This example demonstrates the improved biological activity of peptide constructs according to the present invention in comparison to similar peptide constructs and conventional peptide-immunogenic carrier constructs.

I. Peptides

Peptide constructs were prepared using as T cell binding ligand, either Peptide G' (SEQ ID NO:1), Peptide G (SEQ ID NO:2), Peptide J, from a region of β-2 microglobulin (38-50)

DLL KNG ERI EKV E SEQ ID NO:34

or Peptide F, from IL-1β (163-171)

VQG EES NDK SEQ ID NO:35.

or using a conventional immunogenic carrier protein, Keyhole Limpet Haemocyanin (KLH) (Biosyn).

The peptide constructs are prepared using Peptide J or Peptide F or Peptide G' or Peptide G with the modified HGP-30 having SEQ ID NO:6 (mH) or HGP-30 (YSVHQRIDVKDTKEALEKIEEEQNKSKKKA) (SEQ ID NO:36) and a spacer GGG

(however, similar results would be obtained using a different spacer, e.g., GGGS, GGGSGGGS (SEQ ID NO:93), GGGGSGGGGSGGGGS (SEQ ID NO: 94); GGGSGGSS (SEQ ID NO:95), GGGGSGGGGS (SEQ ID NO:96), etc.).

Accordingly, the peptide constructs used in this example have the following formulas:

DGQ EEK AGV VST GLI GGG ATL YSV HQR IDV KDT KEA LEK IEE EQN KS

SEQ ID NO:37

NGQ EEK AGV VST GLI GGG ATL YSV HQR IDV KDT KEA LEK IEE EQN KS

SEQ ID NO:38

DLL KNG ERI EKV EGG GAT LYS VHQ RID VKD TKE ALE KIE EEQ NKS

SEQ ID NO:39

VQG EES NDK GGG ATL YSV HQR ICV KDT KEA LEK IEE EQN KS

SEQ ID NO:40

wherein the underlined portion represents mH (SEQ ID NO:6); and

VQG EES NDK GGG YSV HQR IDV KDT KEA LEK IEE EQN KSK KKA

SEQ ID NO:41

where the double underlined portion represents HGP-30 (SEQ ID NO:36).

The peptides may be synthesized using, for example, the F-moc or t-Boc procedure and a double coupling protocol for the first 8 residues. Usually the peptide is prepared with the carboxyl terminus as an amide form. All of the peptides are purified using preparative HPLC, and analyzed by an analytical

HPLC, amino acid analysis and mass spectrophotometer. The peptides are greater than 95%, usually greater than 98%, pure by HPLC criteria. The dry peptides are stored in vials with desiccant at -8°C.

II. Preparation of KLH Conjugates

Keyhole Limpet Haemocyanin (KLH) (cGMP grade, Biosyn) is conjugated to m-HGP-30 (mH) peptide by a glutaraldehyde conjugation method using a 1:1 mg weight ratio of peptide to KLH.

The peptide constructs may be synthesized as a single peptide without any conjugation step or by conjugation of the T cell binding ligand peptide (G', G, F or J) and the antigenic peptide (e.g., mH or HGP-30) by using the thioether method or by any other conjugation method known to the skilled practitioner.

The final products (peptides, peptide constructs, peptide -KLH control), are analyzed for protein or peptide using the BCA protein, or other suitable, assay, and adjusted to contain between 200-400 μg/ml of total protein or peptide, and stored frozen (-20°C) in suitable (e.g., 1.5 ml) aliquots ready for thawing and administered in combination with an adjuvant ISA-51 (Seppic) or microfluidized MPL S/E (Corixa).

III. Immunization and Assay Procedures

The procedure used is as described below.

Mice in groups (5-10 animals per group as designated) are immunized with the LEAPS constructs (25 μg/dose) of SEQ ID NO's:37, 38 and 39, in 0.2 mL emulsified 1:1 with adjuvant (Seppic's ISA-51 or Corixa's microfluidized MPL S/E) on days 0

and 14. Mice are evaluated by Delayed Type of Hypersensitivity (DTH) by inoculation on day 26 with 20 μl of a solution of saline or mH (SEQ ID NO:6) (25 μg in saline) in the left or right ear respectively. The DTH response is determined by measurement of the ear thickness 48 hours later and expressed as increase in ear thickness (mm) of experimental ear compared to that of the control ear. Individual animal sera are collected for measurement of antibody on day 28, 42, 63 and 77. Sera from individual animals and group pools are evaluated for specific anti-mH antibody, for total antibody, IgG1, IgG2a and IgG3 antibody isotype and cross clade titer at selected time points as indicated.

IV. Results

The results of an isotype analysis of day 42 test bleedings with G'-mH (SEQ ID NO:37), G-mH (SEQ ID NO:38), J-mH (SEQ ID NO:39), F-mH (SEQ ID NO:40) and F-HGP-30 (SEQ ID NO:41), are shown in Table 1. The G' construct resulted in significantly higher signals, indicative of higher levels of the TH1 preferred isotypes (IgG2a and IgGb2) relative to the TH2 isotypes (IgG1).

Table 2 shows the results of the ELISA antibody screening of the sera from the above animals, but with test bleeding collected at day 63 and for cross clade recognition. The mouse sera for the ELISA was used at a dilution of 1:200. Again, clearly, the

construct provides higher signals indicative of higher levels of the antibodies that recognized other clades besides the parental one (Clade B) of mH.

An isotype analysis for pools of day 28 test bleedings G-mH, G'-mH and m-HGP-30/KLH using either MPL S/E or ISA51 as adjuvant, are shown in Table 3. These results from another group of animals confirm the results in Table 1 and extend the observation by showing higher endpoint titers for the preferred isotypes.

A cross clade analysis for pools of day 42 test bleedings from the same groups as used in Table 3, were obtained and the results are shown in Table 4. Clearly the G' construct resulted in higher signals indicative of higher levels of the TH1 preferred antibody isotypes (IgG2a and IgG2b) relative to the TH2 antibody isotypes (IgG1). Again, clearly, the G' construct resulted in higher signals indicative of higher levels of the antibodies that recognized other clades besides the parental one (Clade B) of the mH, although not as strong as the KLH conjugates.

A specificity analysis for the TCBL or KLH carrier for pools of day 42 test bleedings from the G-mH, G'-mH and mH/KLH, using either MPL S/E or ISA51 as adjuvant, was carried out (all sera assayed at a dilution of 1:200) and the results are shown in Table 5. These results demonstrate that G' conjugates and the G conjugate showed minimal reactivity toward the delivery vehicle

TCBL as contrasted to the KLH conjugates. This observation is especially significant for vaccines used on a repetitive basis, such as, either a vaccine that requires more frequent intervals between boosters for maintenance of cellular reactivity or as a therapeutic vaccine.

Example 2

This example is designed to demonstrate "mechanism of action" as further "proof of principle" of the LEAPS technology. The analysis is based on use of peptide J with mH (SEQ ID NO:39) and Peptide G' with mH (SEQ ID NO:37), for mechanism and types of cells involved.

Select immunoglobulin preparations were obtained from Dr. Stephen Hoffmann, Malaria Program, U.S. Navy. These preparations were prepared using specialized monoclonal antibodies (anti CD4 or CD8) that allow the determination by depletion of the cell type that possess the markers the antibodies recognize. This allows one to determine some parts of the nature of various cellular (e.g., T-cell) involvement in the early stage of immune system response with the LEAPS peptide-constructs. It is recognized, however, that this is only a temporary event since new cells are continuously being developed from stem cells and the animals become resistant to the reagents.

The animals are pretreated with the antisera as indicated for 5 days before the initial immunization with peptide-construct having SEQ ID NO:37 or SEQ ID NO:39 on day 1. No pretreatment is done before the booster immunization on day 14 or DTH on day

26-28. The mice are then inoculated with the test antigen or saline (control) on day 26 in the left and right ears, respectively, and the DTH response is measured on day 28. The difference between the values for the test and saline control ears is calculated for each group of five animals along with the standard error of the mean (sem) and the results are plotted (see Fig. 1). Also shown in Fig. 1 are values for the untreated animals and animals immunized on day 14 only.

These initial results, as shown in Fig. 1, using the cell specific antisera as a depletion reagent (used to eliminate from the mouse functional cells that contain a specific surface marker) for the primary immunization, demonstrate that for a DTH response: (1) SEQ ID NO:37 construct requires the presence and presumably activation of CD4+ but not CD8+ cells, and (2) SEQ ID NO:59 construct containing a TCBL from β-2-microglobulin which is associated with MHC I, requires the presence and presumably activation of CD8+ but not CD4+ cells. The DTH (Delayed Type Hypersensitivity) data is statistically significant with a t-test of 0.05 for SEQ ID NO:39 and anti-CD8. The DTH for pretreatment of SEQ ID NO:37 immunized mice with anti-CD4 was just above the cutoff limit for statistical significance due to a weaker DTH response and small group size. Table 6 shows the same DTH data and provides additional experimental details.

Example 3

This example is similar to Example 2 but using a more sensitive ELISA test for antibody type. As shown in Fig. 2 the SEQ ID NO:37 antisera depletion was statistically significant (p=0.002) because pretreatment with anti-CD4 completely eliminated any antibodies from being detected at a time when they were detected in control animals (untreated or treated with normal rat IgG). This was not the case, however, with pretreatment using anti-CD8 or normal rat IgG. No antibody data is shown for SEQ ID NO:39, as for this type of MHC-I TCBL construct day 28 is too early to detect any antibodies to the immunogen.

PEPTIDE CONSTRUCT	Mouse #	IgG1	IgG2a	IgG2b	IgG3
SEQ ID NO:58	4524	1.738	0.074	0.464	0.033
	4525	0.123	0.005	0.017	-0.013
	4526	1.649	0.129	0.025	0.152
	4527	2.651	1.619	1.613	2.378
	4528	0.562	0.047	0.059	0.000
	4529	0.431	0.031	0.038	0.106
	4530	0.042	0.025	0.183	0.089
	4531	2.391	0.200	0.123	0.358
	4532	1.810	0.152	0.223	0.388
	4533	2.606	1.386	2.038	1.817
	Average	1.400	0.367	0.478	0.531
SEQ ID NO:57	4534	2.577	1.399	2.050	1.853
	4535	2.623	1.302	1.588	1.268
	4536	2.588	1.630	1.735	1.856
	4537	2.601	0.467	0.534	1.229
	4538	2.757	1.249	1.261	2.186
	4539	2.886	2.275	2.717	1.921
	4540	2.768	0.998	1.656	1.276
	4541	2.574	1.693	2.009	2.181
	4542	2.628	1.693	1.613	0.672
	4543	2.671	1.566	1.785	1.183
	Average	2.667	1.427	1.695	1.562
SEQ ID NO:62	4544	0.792	0.022	0.031	0.490
	4545	0.184	0.010	0.009	0.014
	4547	0.742	0.323	0.610	0.597
	4548	0.194	0.033	0.007	0.016
	4549	0.095	0.003	0.000	0.009
	4550	0.072	0.003	0.008	0.041
	4551	0.023	0.000	0.005	0.079
	4552	0.115	0.000	0.000	0.001
	4553	0.095	0.007	0.000	0.016
	Average	0.257	0.044	0.074	0.140
SEQ ID NO: 63	4554	0.761	0.051	0.003	0.040
	4555	0.181	0.018	0.001	0.006
	4556	0.649	0.020	0.007	0.104
	4557	0.417	0.007	0.005	0.173
	4558	0.022	0.000	0.006	0.009
	4559	1.379	0.000	0.028	0.013
	4560	0.030	0.048	0.047	0.007
	4561	0.349	0.026	0.000	0.000
	4562	0.717	0.192	0.027	0.058
	4563	2.018	0.350	0.117	0.028
	Average	0.652	0.071	0.024	0.044
SEQ ID NO: 59	4564	0.002	0.002	0.002	0.017
	4565	1.603	0.027	0.014	0.032
	4566	0.014	0.000	0.000	0.009
	4567	2.023	0.299	0.113	0.227
	4568	2.199	0.060	0.039	0.324
	4569	0.053	0.002	0.000	0.000
	4570	0.057	0.014	0.000	0.003
	4571	0.505	0.011	0.000	0.016
	4572	0.000	0.000	0.000	0.000
	Average	0.717	0.046	0.019	0.070

Group	Mouse #	modified HGP-30	B Clade	C Clade	D Clade	E Clade
SEQ ID NO:58	4524	1.740	0.000	0.047	0.001	0.000
	4525	0.398	0.000	0.005	0.000	0.000
	4526	1.240	0.006	0.076	0.016	0.000
	4527	2.665	0.230	0.643	0.000	0.504
	4528	1.014	0.000	0.000	0.000	0.000
	4529	0.444	0.000	0.000	0.000	0.000
	4530	0.304	0.000	0.000	0.000	0.000
	4531	1.831	0.000	0.125	0.025	0.000
	4532	2.453	0.316	0.359	0.646	0.000
	4533	2.530	0.148	0.238	0.000	0.018
SEQ ID NO:57	4534	2.737	1.667	1.454	1.527	0.933
	4535	2.471	0.160	0.127	0.438	0.030
	4536	2.569	0.099	0.427	0.408	0.113
	4537	2.093	0.236	0.073	0.125	0.041
	4538	2.512	1.547	1.592	1.471	0.000
	4539	3.115	0.470	0.651	0.772	0.029
	4540	3.153	1.138	1.365	1.328	0.068
	4541	2.922	0.994	1.139	1.370	0.006
	4542	2.236	0.000	0.008	0.000	0.000
	4543	2.534	0.505	1.191	0.374	0.271
SEQ ID NO:62	4544	0.525	0.255	0.135	0.216	0.014
	4545	0.137	0.016	0.014	0.000	0.000
	4547	1.736	0.918	0.570	1.126	0.365
	4548	0.143	0.004	0.106	0.000	0.000
	4549	0.077	0.006	0.055	0.007	0.000
	4550	0.158	0.000	0.000	0.001	0.000
	4551	0.033	0.011	0.032	0.009	0.000
	4552	0.121	0.013	0.068	0.000	0.000
	4553	0.226	0.000	0.000	0.000	0.000
SEQ ID NO:63	4554	0.065	0.000	0.000	0.000	0.000
	4555	0.216	0.282	0.135	0.012	0.000
	4556	0.128	0.000	0.000	0.000	0.000
	4557	0.000	0.000	0.000	0.005	0.000
	4558	0.110	0.000	0.000	0.000	0.000
	4559	0.017	0.000	0.000	0.000	0.000
	4560	0.201	0.000	0.010	0.000	0.000
	4561	0.623	1.977	1.878	1.941	1.585
	4562	0.747	0.667	0.650	0.386	0.042
	4563	0.013	0.011	1.051	0.050	1.010
SEQ ID NO:59	4564	0.440	0.282	2.421	0.120	2.431
	4565	0.011	0.000	1.699	0.004	1.585
	4566	0.753	0.575	1.295	0.196	0.789
	4567	0.905	0.026	0.969	0.000	0.788
	4568	0.793	0.000	0.665	0.000	0.554
	4569	0.100	0.000	0.780	0.000	0.722
	4570	0.035	0.000	0.171	0.000	0.142
	4571	0.000	0.000	1.370	0.000	1.379
	4572	0.000	0.000	2.322	0.000	2.379

OF LEAPS MODIFIED HGP-30 IMMUNIZED MICE USING PEPTIDE G OR A DERIVATIZED FORM AS TCBL

Group	Isotype	Serial Dilution 1:200	1:800	1:3200	1:12800	1:51200	1:204800
SEQ ID NO:58 (with MPL)	Ig1	0.103	0.022	0.003	0.000	0.000	0.000
	Ig2a	0.248	0.048	0.000	0.000	0.002	0.000
	Ig2b	0.147	0.026	0.022	0.006	0.007	0.018
	Ig3	0.265	0.044	0.006	0.001	0.000	0.000
SEQ ID NO:57 (with MPL)	Ig1	2.642	1.638	0.652	0.279	0.091	0.014
	Ig2a	1.961	0.899	0.263	0.081	0.028	0.005
	Ig2b	1.872	0.881	0.253	0.104	0.011	0.006
	Ig3	1.965	0.805	0.215	0.045	0.005	0.000
SEQ ID NO:58	Ig1	0.507	0.173	0.025	0.009	0.014	0.000
	Ig2a	0.000	0.015	0.000	0.003	0.006	0.000
	Ig2b	0.017	0.000	0.004	0.001	0.000	0.000
	Ig3	0.009	0.002	0.000	0.000	0.000	0.000
SEQ ID NO:57	Ig1	3.006	2.441	1.755	1.069	0.367	0.114
	Ig2a	0.729	0.218	0.068	0.025	0.015	0.008
	Ig2b	1.420	0.505	0.134	0.054	0.014	0.000
	Ig3	1.132	0.358	0.092	0.020	0.004	0.000
KLH-m-HGP-30	Ig1	2.693	1.582	0.621	0.294	0.065	0.000
	Ig2a	2.276	0.980	0.330	0.115	0.015	0.003
	Ig2b	2.284	1.069	0.344	0.169	0.018	0.009
	Ig3	0.903	0.235	0.040	0.003	0.001	0.000
KLH-m-HGP-30	Ig1	3.161	2.695	1.807	1.043	0.256	0.091
	Ig2a	2.241	1.049	0.458	0.165	0.014	0.000
	Ig2b	2.103	0.778	0.175	0.108	0.024	0.004
	Ig3	0.550	0.185	0.022	0.017	0.000	0.002

Group		ELISA TEST ANTIGENS				
		Modified HGP-30	B Clade	C Clade	D Clade	E Clade
SEQ ID NO:58 (A)	4637	0.470	0.000	0.000	0.000	0.000
	4638	1.103	0.000	0.000	0.000	0.000
	4639	0.046	0.000	0.000	0.000	0.000
	4640	0.390	0.000	0.004	0.000	0.000
	4641	1.297	0.028	0.104	0.000	0.000
	4642	0.153	0.000	0.000	0.000	0.000
	Group Average	0.576	0.005	0.018	0.000	0.000
SEQ ID NO:57 (A)	4643	2.307	0.271	0.616	0.052	0.092
	4644	1.589	0.000	0.000	0.000	0.000
	4645	2.432	0.036	0.518	0.010	0.000
	4646	2.867	0.507	0.920	0.000	0.018
	4647	2.627	0.187	0.767	0.003	0.101
	4648	2.780	1.074	1.454	0.114	0.000
	Group Average	2.433	0.346	0.712	0.030	0.035
KLH-m-HGP-30 (A)	4674	3.013	2.768	2.740	0.000	0.000
	4675	2.683	2.555	2.384	0.000	1.697
	4676	2.774	0.842	1.545	0.012	0.135
	4677	2.919	2.443	2.671	0.000	0.351
	4678	2.670	2.566	2.775	0.109	0.461
	Group Average	2.749	1.920	2.138	0.025	0.446
SEQ ID NO:58 (B)	4662	0.187	0.000	0.003	0.005	0.000
	4663	0.188	0.006	0.003	0.006	0.000
	4664	1.848	0.000	0.000	0.000	0.000
	4665	0.145	0.000	0.000	0.000	0.000
	4666	0.000	0.079	0.000	0.000	0.000
	4667	0.000	0.046	0.050	0.000	0.000
	Group Average	0.394	0.022	0.009	0.002	0.000
SEQ ID NO:57 (B)	4668	2.330	2.348	2.575	0.087	0.000
	4669	2.213	0.496	0.837	0.095	0.000
	4670	2.534	1.799	1.711	0.185	0.054
	4671	3.358	1.228	2.254	1.799	0.358
	4672	3.030	2.244	0.911	1.727	0.113
	4673	2.571	0.349	1.070	0.637	0.037
	Group Average	2.672	1.410	1.559	0.755	0.094
KLH-m-HGP-30 (B)	4679	2.852	2.546	2.317	1.648	0.054
	4680	3.484	1.243	2.006	0.094	0.000
	4681	3.374	2.622	2.873	0.000	1.094
	4682	3.262	2.485	2.863	0.324	0.000
	4683	3.009	2.554	2.623	1.383	1.044
	Group Average	3.109	2.143	2.373	0.700	0.381

Group	Animal #	A 490 1:200 dilution on plates coated with modified HGP-30	Peptide G	KLH
SEQ ID NO:58	4637	0.257	0.195	ND
	4638	0.571	0.122	ND
	4639	0.065	0.092	ND
	4640	0.392	0.088	ND
	4641	1.008	0.054	ND
	4642	0.021	0.047	ND
	Average	0.386	0.099	
SEQ ID NO:57	4643	2.178	0.083	ND
	4644	1.411	0.054	ND
	4645	2.314	0.097	ND
	4646	2.555	0.038	ND
	4647	2.404	0.087	ND
	4648	2.273	0.121	ND
	Average	2.189	0.080	
KLH-m-HGP-30	4674	2.825	0.248	>3.5
	4675	2.724	0.186	>3.5
	4676	2.544	0.303	>3.5
	4677	2.862	0.185	>3.5
	4678	2.654	0.150	>3.5
	Average	2.722	0.214	>3.5
SEQ ID NO:58	4662	0.051	0.024	ND
	4663	0.052	0.044	ND
	4664	1.102	0.062	ND
	4665	0.005	0.033	ND
	4666	0.000	0.060	ND
	4667	0.000	0.151	ND
	Average	0.202	0.062	
SEQ ID NO:57	4668	1.968	0.091	ND
	4669	1.422	0.024	ND
	4670	1.755	0.006	ND
	4671	2.450	0.015	ND
	4672	2.403	0.126	ND
	4673	1.399	0.113	ND
	Average	1.899	0.062	
KLH-m-HGP-30	4679	2.701	0.171	>3.5
	4680	2.177	0.057	>3.5
	4681	2.397	0.167	>3.5
	4682	2.489	0.028	>3.5
	4683	2.108	0.032	>3.5
	Average	2.374	0.091	>3.5

TABLE 6 - DETERMINATION OF TYPE OF CELLS INVOLVED IN DTH RESPONSE TO MODIFIED HGP-30 BY LEAPS IMMUNIZED MICE BY ANTISERA DEPLETION OF CD4 OR CD8 CELLS

Treatment*		SEQ ID NO:57 (with MHC II TCBL for CD4)			SEQ ID NO:58 (with MHC I TCBL for CD8)		
DTH Parameters Ear inoculated day 26 with Ear thickness measured after 48 hours		Right Ear saline mm	Left Ear HGP-30 mm	% increase (L-R)/R	Right Ear saline mm	Left Ear HGP-30 mm	% increase (L-R)/R
None	Average of group (5 mice)	0.224	0.274	22.10%	0.222	0.288	29.30%
Normal rat IgG	Average of group (5 mice)	0.232	0.278	19.90%	0.227	0.296	30.60%
Anti CD4	Average of group (5 mice)	0.237	0.252	6.10%	0.240	0.288	20.00%
Anti CD8	Average of group of 5 mice	0.232	0.290	25.00%	0.220	0.233	6.20%***
Day 14** Injection Only	Average of group of 5 mice	0.222	0.234	5.10%	0.231	0.254	10.00%

* animals were treated with antisera daily for 5 days before initiation of immunizations on days 1 and 14 with LEAPS construct and ISA 51 adjuvant

**animals were only immunized with LEAPS construct on day 14

*** t test $p<0.05$

What is claimed is:

Claim 1. A peptide having the sequence of SEQ ID NO:1.

Claim 2. A peptide construct capable of eliciting a cellular immune response when administered to a patient in need thereof, said peptide construct comprising a first T cell specific binding peptide and a second T cell specific binding peptide, said first and second peptides being derived from different molecules and covalently linked together, wherein said first T cell specific binding peptide binds to a specific class or subclass of T cells and has the sequence of SEQ ID NO:1, and said second T cell specific binding peptide is an antigenic peptide capable of eliciting TH1 associated antibodies, and wherein said first and second peptides are covalently linked to each other directly or via a spacer.

Claim 3. The peptide construct of claim 2 wherein the antigenic peptide is a peptide having sequence identity with the p17 gag protein of HIV-1 wherein the peptide has a sequence originating with an amino acid residue chosen from residues chosen from residues 76 to 83 and ending with an amino acid residue chosen from residues 107 to 112 of p17 gag protein of HIV-1.

Claim 4. The peptide construct of claim 3 having SEQ ID NO:37.

Claim 5. An immunogenic composition comprising the peptide construct of claim 2 or 3 and an immunogenic carrier.

Claim 6. An immunogenic composition comprising the peptide construct having SEQ ID NO:37 and an immunogenic carrier.

Claim 7. A method of eliciting a cellular immune response in a human patient in need thereof, comprising administering to said patient an immunologically effective amount of the peptide construct of claim 2 or 3.

Claim 8. The method of claim 7 wherein the peptide construct is administered in combination with an immune response adjuvant.

Claim 9. A method of eliciting a cellular immune response in a human patient exposed to or at risk for exposure to the AIDS virus, comprising administering to said patient an immunologically effective amount of a conjugated peptide having SEQ ID NO:37.

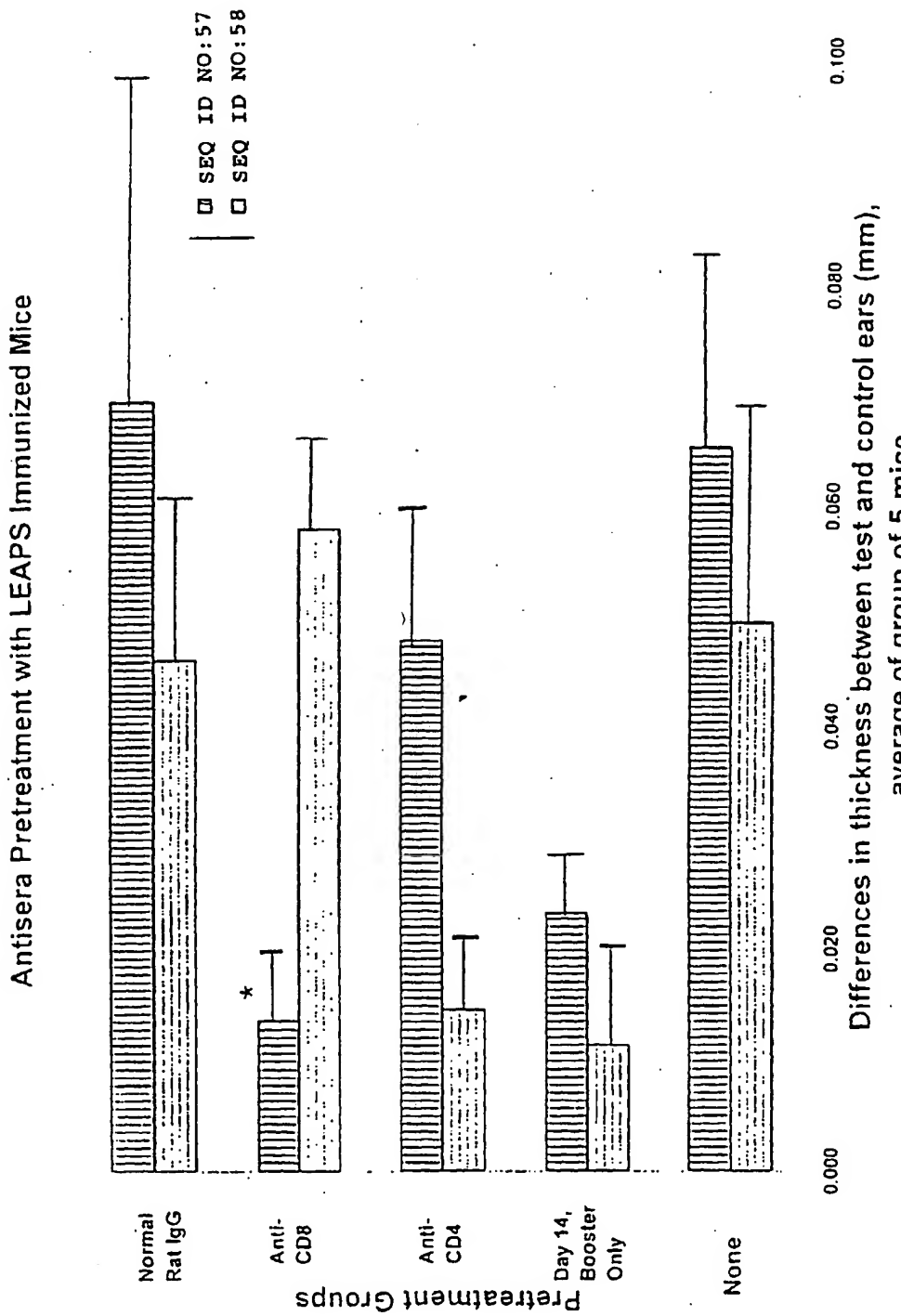
Antisera Pretreatment with LEAPS Immunized Mice
SEQ ID NO:57
SEQ ID NO:58
*
Normal Rat IgG
Anti-CD8
Anti-CD4
Day 14, Booster Only
None
Pretreatment Groups
0.000
0.020
0.040
0.060
0.080
0.100
Differences in thickness between test and control ears (mm), average of group of 5 mice

FIGURE 1

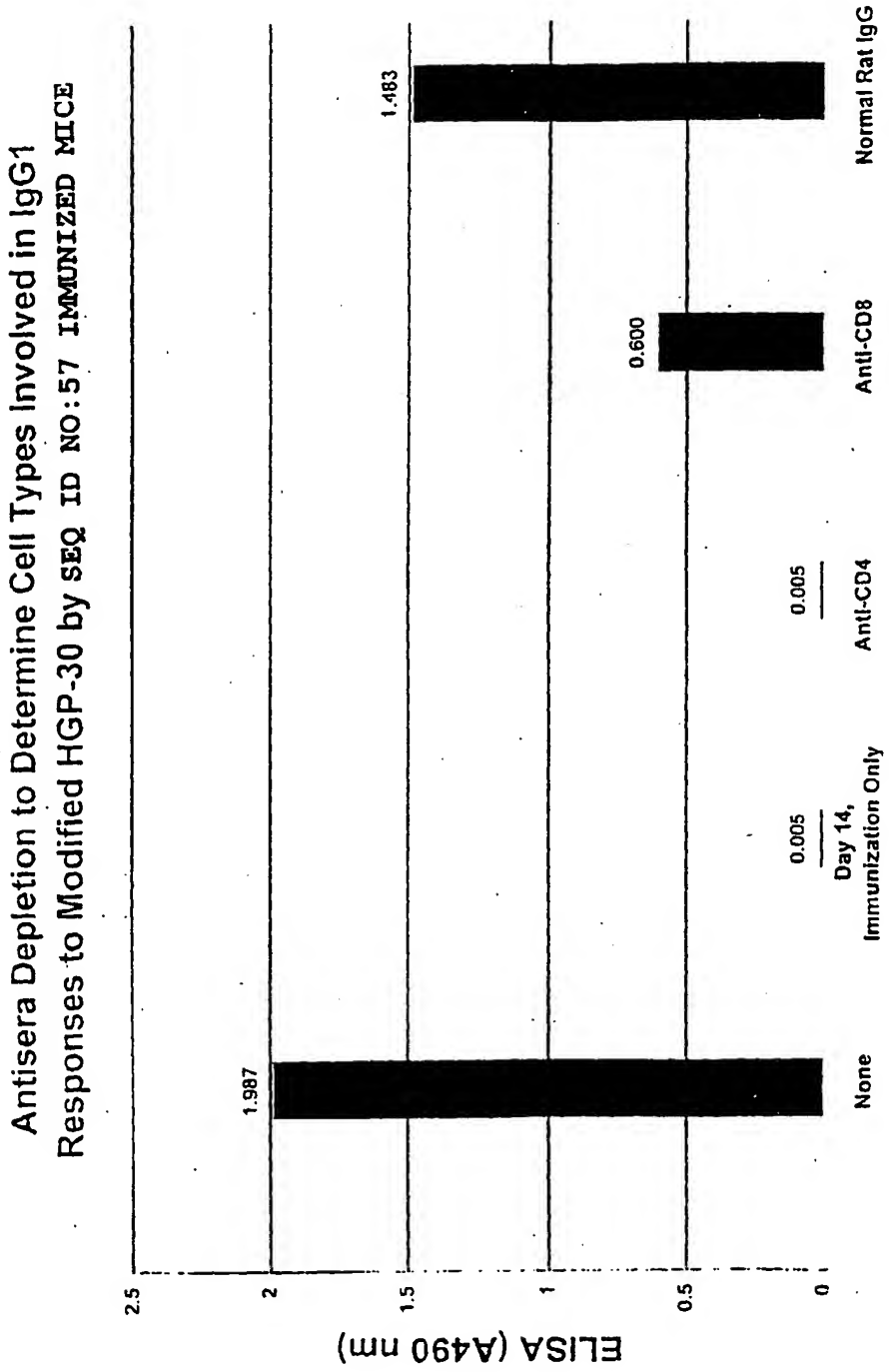
Antisera Depletion to Determine Cell Types Involved in IgG1
Responses to Modified HGP-30 by SEQ ID NO:57 IMMUNIZED MICE
ELISA (A490 nm)
2.5
2
1.5
1
0.5
0
1.987
1.483
0.600
None
Anti-CD4
Anti-CD8
Normal Rat IgG
0.005
Day 14,
Immunization Only
0.005
Pretreatment Group

FIGURE 2

Raw Sequence Listing

Sequence Listing

(1) GENERAL INFORMATION:

(i) APPLICANT:CELL-SCI CORPORATION

(ii) TITLE OF INVENTION:T CELL BINDING LIGAND PEPTIDES, PEPTIDE CONSTRUCTS CONTAINING SAME AND USE THEREOF FOR TREATMENT OF IMMUNOLOGICAL DISORDERS

(iii) NUMBER OF SEQUENCES:96

(iv) CORRESPONDENCE ADDRESS:

(A) ADDRESSEE:Law Office of Sherman and Shalloway

(B) STREET:413 N. Washington Street

(C) CITY:Alexandria

(D) STATE:Virginia

(E) COUNTRY:USA

(F) ZIP:22313

(v) COMPUTER READABLE FORM:

(A) MEDIUM TYPE:Diskette, 3.25 inch, 1.4 mb storage

(B) COMPUTER:Dell Optiplex GX110; 733 MHz Microprocessor

(C) OPERATING SYSTEM:Windows 98

(D) SOFTWARE:Word 2000

(vi) CURRENT APPLICATION DATA:

(A) APPLICATION NUMBER:UNASSIGNED

(B) FILING DATE:CONCURRENTLY HEREWITH

(vii) ATTORNEY/AGENT INFORMATION:

(A) NAME:Richard A. Steinberg

(B) REGISTRATION NUMBER:26,588

(C) REFERENCE/DOCKET NUMBER:CS-112/PCT

(ix) TELECOMMUNICATION INFORMATION:

(A) TELEPHONE:(703) 549-2282

(B) TELEFAX:(703) 836-0106

(2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:15

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:Peptide G'

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:1:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile

5 10 15

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:15

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:Peptide G'

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:MHC II β chain residues 135-149

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:2:

Asn Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile

5 10 15

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:25

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 3:

Ala Thr Leu Tyr Ser Val His Gln Arg Ile Asp Val Lys Asp Thr
5 10 15

Lys Glu Ala Leu Glu Lys Ile Glu Glu Glu
20 25

(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:36

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:4:

Ser Leu Tyr Asn Thr Val Ala Thr Leu Tyr Ser Val His Gln Arg
5 10 15

Ile Asp Val Lys Asp Thr Lys Glu Ala Leu Glu Lys Ile Glu Glu
20 25 30

Glu Gln Asn Lys Ser Lys
35

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:37

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 5:

Arg Ser Leu Tyr Asn Thr Val Ala Thr Leu Tyr Ser Val His Gln
5 10 15

Arg Ile Asp Val Lys Asp Thr Lys Glu Ala Leu Glu Lys Ile Glu
20 25 30

Glu Glu Gln Asn Lys Ser Lys
35

(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:29

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:6:

Ala Thr Leu Tyr Ser Val His Gln Arg Ile Asp Val Lys Asp Thr
5 10 15

Lys Glu Ala Leu Glu Lys Ile Glu Glu Glu Gln Asn Lys Ser
20 25

(2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:37

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 7:

Lys Ser Leu Phe Asn Thr Val Ala Thr Leu Tyr Cys Val His Gln Arg
5 10

Ile Asp Val Lys Asp Thr Lys Glu Ala Leu Asp Lys Ile Glu Glu Ile
20 25 30

Gln Asn Lys Ser Lys
35

(2) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:37

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:8:

Arg Ser Leu Tyr Asn Thr Val Ala Thr Leu Tyr Cys Val His Gln Arg
5 10 15

Ile Glu Val Lys Asp Thr Lys Glu Ala Leu Asp Lys Ile Glu Glu Glu
20 25 30

Gln Asn Lys Ser Lys
35

(2) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:37

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 9:

Arg Ser Leu Xaa Asn Thr Val Ala Thr Leu Tyr Cys Val His Xaa Xaa
5 10 15

Ile Glu Val Arg Asp Thr Lys Glu Ala Leu Asp Lys Ile Glu Glu Glu
20 25 30

Gln Asn Lys Xaa Gln
35

(2) INFORMATION FOR SEQ ID NO: 10:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:37

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:10:

Lys Ser Leu Xaa Asn Thr Val Ala Thr Leu Tyr Cys Val His Glu Arg
5 10 15

Ile Glu Val Lys Asp Thr Lys Glu Ala Leu Glu Lys Met Glu Glu Glu
20 25 30

Gln Asn Lys Ser Lys
35

(2) INFORMATION FOR SEQ ID NO: 11:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:37

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 11:

Arg Ser Leu Tyr Asn Thr Val Ala Val Leu Tyr Phe Val His Gln Arg
5 10 15

Val Glu Val Lys Asp Thr Lys Glu Ala Leu Asp Lys Leu Glu Glu Glu
20 25 30

Gln Asn Lys Ser Gln
35

(2) INFORMATION FOR SEQ ID NO: 12:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:37

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:12:

Lys Ser Leu Xaa Asn Xaa Xaa Ala Xaa Leu Xaa Cys Xaa His Gln Arg
5 10 15

Ile Glu Val Lys Asp Thr Lys Glu Ala Leu Glu Glu Val Glu Lys Ala
20 25 30

Gln Lys Asn Ser Gln
35

(2) INFORMATION FOR SEQ ID NO: 13:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:37

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 13:

Gln Ser Leu Phe Asn Leu Leu Ala Xaa Leu Tyr Cys Val His Gln Arg
5 10 15

Ile Asp Xaa Lys Asp Thr Lys Glu Ala Leu Xaa Lys Xaa Xaa Glu Xaa
20 25 30

Gln Asn Xaa Xaa Gln
35

(2) INFORMATION FOR SEQ ID NO: 14:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:37

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:14:

Xaa Ser Leu Trp Asn Ala Ile Xaa Val Leu Trp Cys Val His Asn Arg
5 10 15

Xaa Xaa Ile Xaa Asp Thr Gln Gln Ala Ile Gln Lys Leu Lys Glu Val
20 25 30

Met Xaa Ser Arg Lys
35

(2) INFORMATION FOR SEQ ID NO: 15:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:28

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 15:

Lys Ser Leu Phe Asn Thr Val Ala Val Leu Tyr Cys Val His Gln Arg
5 10 15

Ile Glu Val Lys Asp Thr Lys Glu Ala Leu Asp Lys
20 25

(2) INFORMATION FOR SEQ ID NO: 16:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:30

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:16:

Tyr Cys Val His Gln Lys Ile Glu Val Lys Asp Thr Lys Glu Ala Leu
5 10 15

Glu Lys Ile Glu Glu Glu Gln Asn Lys Ser Lys Lys Lys Ala
20 25 30

(2) INFORMATION FOR SEQ ID NO: 17:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:30

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 17:

Trp Cys Val His Gln Arg Ile Glu Val Lys Asp Thr Lys Glu Ala Leu
5 10 15

Asp Lys Ile Glu Glu Val Gln Asn Lys Ser Gln Gln Lys Thr
20 25 30

(2) INFORMATION FOR SEQ ID NO: 18:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:30

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:18:

Tyr Cys Val His Gln Arg Ile Asp Val Lys Asp Thr Lys Glu Ala Leu
5 10 15

Asn Lys Ile Glu Glu Met Gln Asn Lys Asn Lys Gln Arg Thr
20 25 30

(2) INFORMATION FOR SEQ ID NO: 19:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:30

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 19:

Tyr Cys Val His Gln Arg Ile Asp Val Lys Asp Thr Lys Glu Ala Leu
5 10 15

Asp Lsy Ile Glu Glu Ile Gln Asn Lys Ser Lys Gln Lys Thr
20 25 30

(2) INFORMATION FOR SEQ ID NO: 20:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:30

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:20:

Tyr Phe Val His Gln Arg Val Glu Val Lys Asp Thr Lys Glu Ala Leu
5 10 15

Asp Lys Leu Glu Glu Glu Gln Asn Lys Ser Gln Gln Lys Thr
20 25 30

(2) INFORMATION FOR SEQ ID NO: 21:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:30

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 21:

Tyr Cys Val His Gln Lys Ile Asp Val Arg Asp Thr Lys Glu Ala Leu
5 10 15

Glu Lys Val Glu Glu Glu Gln Asn Lys Ser Lys Glu Lys Ala
20 25 30

(2) INFORMATION FOR SEQ ID NO: 22:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:30

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:22:

Tyr Cys Val His Gln Arg Ile Asp Val Lys Asp Thr Lys Glu Ala Leu
5 10 15

Asp Lys Ile Glu Glu Glu Gln Asn Lys Ser Lys Lys Lys Glu
20 25 30

(2) INFORMATION FOR SEQ ID NO: 23:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:30

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 23:

Tyr Cys Val His Lys Gly Ile Glu Val Arg Asp Thr Lys Glu Ala Leu
5 10 15

Asp Lys Ile Glu Glu Glu Gln Asn Lys Ile Gln Gln Lys Thr
20 25 30

(2) INFORMATION FOR SEQ ID NO: 24:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:30

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:24:

Tyr Cys Val His Xaa Xaa Ile Glu Val Arg Asp Thr Lys Glu Ala Leu
5 10 15

Asp Lys Ile Glu Glu Glu Gln Asn Lys Xaa Gln Gln Lys Thr
20 25 30

(2) INFORMATION FOR SEQ ID NO: 25:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:30

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:25:

Tyr Cys Val His Glu Arg Ile Lys Val Ala Asp Thr Lys Glu Ala Leu
5 10 15

Asp Lys Ile Glu Glu Glu Gln Thr Lys Ser Lys Lys Lys Ala
20 25 30

(2) INFORMATION FOR SEQ ID NO: 26:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:37

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 26:

Arg Ser Leu Tyr Asn Thr Val Ala Thr Leu Tyr Cys Val His Gln Arg
5 10 15

Ile Asp Val Lys Asp Thr Lys Glu Ala Leu Glu Lys Ile Glu Glu Glu
20 25 30

Lys Gln Lys Ser Lys
35

(2) INFORMATION FOR SEQ ID NO: 27:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:37

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:27:

Lys Ser Leu Tyr Asn Thr Val Ala Thr Leu Tyr Cys Val His Gln Lys
5 10 15

Ile Glu Ile Lys Asp Thr Lys Glu Ala Leu Glu Lys Ile Glu Glu Glu
20 25 30

Gln Asn Lys Ser Lys
35

(2) INFORMATION FOR SEQ ID NO: 28:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:6

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 28:

Gly Gly Gly Gly Ser Ser
5

(2) INFORMATION FOR SEQ ID NO: 29:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:12

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:29:

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly

5 10

(2) INFORMATION FOR SEQ ID NO: 30:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:12

(B) TYPE:amino acid

(C) TOPOLOGY:

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 30:

Gly Gly Gly Ser Gly Thr Gly Ser Gly Ser Gly Ser

5 10

(2) INFORMATION FOR SEQ ID NO: 31:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:13

(B) TYPE:amino acid

(C) TOPOLOGY:

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:31:

Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser

5 10

(2) INFORMATION FOR SEQ ID NO: 32:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:7

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 32:

Lys Gly Lys Gly Lys Gly Leu

5

(2) INFORMATION FOR SEQ ID NO: 33:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:19

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:33:

Val Ala Lys Leu Glu Ala Lys Val Ala Lys Leu Glu Ala Lys Gly Lys Gly Lys Tyr
5 10 15

(2) INFORMATION FOR SEQ ID NO: 34:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:13

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:β-2 microglobulin Peptide J

(B) LOCATION:38-50

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 34:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu
5 10

(2) INFORMATION FOR SEQ ID NO: 35:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:9

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:Interleukin 1β, Peptide F

(B) LOCATION:163-171

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:35:

Val Gln Gly Glu Glu Ser Asn Asp Lys

5

(2) INFORMATION FOR SEQ ID NO: 36:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:30

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:HIV p17 HGP30

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 36:

Tyr Ser Val His Gln Arg Ile Asp Val Lys Asp Thr Lys Glu Ala Leu

5 10 15

Glu Lys Ile Glu Glu Glu Gln Asn Lys Ser Lys Lys Lys Ala

20 25 30

(2) INFORMATION FOR SEQ ID NO: 37:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:47

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:37:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Ala Thr Leu Tyr Ser Val His Gln Arg Ile Asp Val Lys Asp
20 25 30

Thr Lys Glu Ala Leu Glu Lys Ile Glu Glu Glu Gln Asn Lys Ser
35 40 45

(2) INFORMATION FOR SEQ ID NO: 38:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:47

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 38:

Asn Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Ala Thr Leu Tyr Ser Val His Gln Arg Ile Asp Val Lys Asp
20 25 30

Thr Lys Glu Ala Leu Glu Lys Ile Glu Glu Glu Gln Asn Lys Ser
35 40 45

(2) INFORMATION FOR SEQ ID NO: 39:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:45

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:39:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Ala Thr Leu Tyr Ser Val His Gln Arg Ile Asp Val Lys Asp Thr Lys
20 25 30

Glu Ala Leu Glu Lys Ile Glu Glu Glu Gln Asn Lys Ser
35 40 45

(2) INFORMATION FOR SEQ ID NO: 40:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:41

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 40:

Val Gln Gly Glu Glu Ser Asn Asp Lys Gly Gly Gly Ala Thr Leu Tyr
5 10 15

Ser Val His Gln Arg Ile Cys Val Lys Asp Thr Lys Glu Ala Leu Glu
20 25 30

Lys Ile Glu Glu Glu Gln Asn Lys Ser
35 40

(2) INFORMATION FOR SEQ ID NO: 41:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:42

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:41:

Val Gln Gly Glu Glu Ser Asn Asp Lys Gly Gly Gly Tyr Ser Val His
5 10 15

Gln Arg Ile Asp Val Lys Asp Thr Lys Glu Ala Leu Glu Lys Ile Glu
20 25 30

Glu Glu Gln Asn Lys Ser Lys Lys Lys Ala
35 40

(2) INFORMATION FOR SEQ ID NO: 42:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:19

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:Peptide My

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 42:

Asp Ser Ala Phe Asp Val Leu Ser Phe Thr Ala Glu Glu Lys Ala Gly
5 10 15

Val Tyr Lys

(2) INFORMATION FOR SEQ ID NO: 43:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:8

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:Muc1 Peptide M1a

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:43:

Ala Pro Asp Thr Arg Pro Ala Pro
5

(2) INFORMATION FOR SEQ ID NO: 44:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:9

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:Muc1 Peptide M1b

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 44:

Ser Thr Ala Pro Pro Ala His Gly Val

5

(2) INFORMATION FOR SEQ ID NO: 45:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:20

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:Muc1 Peptide M1c

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(D) OTHER INFORMATION:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:45:

Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala
5 10 15

Pro Pro Ala His
20

(2) INFORMATION FOR SEQ ID NO: 46:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:9

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:CEA Peptide C1

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 46:

Tyr Ser Leu Gly Ala Asn Leu Asn Leu
5

(2) INFORMATION FOR SEQ ID NO: 47:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:8

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:CEA Peptide C2

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 47:

Glu Ala Gln Asn Thr Thr Tyr Leu

5

(2) INFORMATION FOR SEQ ID NO: 48:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:10

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:CEA Peptide C3

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 48:

Gln Tyr Ser Trp Phe Val Asn Gly Thr Phe

5 10

(2) INFORMATION FOR SEQ ID NO: 49:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:9

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:CEA Peptide C4

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 49:

Thr Tyr Ala Cys Phe Val Ser Asn Leu

5

(2) INFORMATION FOR SEQ ID NO: 50:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:9

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:CEA Peptide C5

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 50:

Ile Tyr Pro Asn Ala Ser Leu Leu Ile

5

(2) INFORMATION FOR SEQ ID NO: 51:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:16

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:Herpes Simplex Virus gD1

(B) LOCATION:8-23

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 51:

Ser Leu Lys Met Ala Asp Pro Asn Arg Phe Arg Gly Lys Asp Leu Pro
5 10 15

(2) INFORMATION FOR SEQ ID NO: 52:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:23

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:Herpes Simplex Virus gD1

(B) LOCATION:1-23

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 52:

Lys Tyr Ala Leu Ala Asp Ala Ser Leu Lys Met Ala Asp Pro Asn Arg
5 10 15

Phe Arg Gly Lys Asp Leu Pro
20

(2) INFORMATION FOR SEQ ID NO: 53:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:22

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:Herpes Simplex Virus extg B1

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 53:

Glu Arg Ile Lys Thr Thr Ser Ser Ile Glu Phe Ala Arg Leu Gln Phe
5 10 15

Thr Thr Asp His Ile Gln
20

(2) INFORMATION FOR SEQ ID NO: 54:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:26

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 54:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Ala Pro Asp Thr Arg Pro Ala Pro
20 25

(2) INFORMATION FOR SEQ ID NO: 55:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:27

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 55:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Ser Thr Ala Pro Pro Ala His Gly Val
20 25

(2) INFORMATION FOR SEQ ID NO: 56:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:38

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 56:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser
20 25 30

Thr Ala Pro Pro Ala His
35

(2) INFORMATION FOR SEQ ID NO: 57:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:27

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 57:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Tyr Leu Ser Gly Ala Asn Leu Asn Leu
20 25

(2) INFORMATION FOR SEQ ID NO: 58:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:26

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 58:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Glu Ala Gln Asn Thr Thr Tyr Leu
20 25

(2) INFORMATION FOR SEQ ID NO: 59:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:28

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 59:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Gln Tyr Ser Trp Phe Val Asn Gly Thr Phe
20 25

(2) INFORMATION FOR SEQ ID NO: 60:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:27

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 60:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Thr Tyr Ala Cys Phe Val Ser Asn Leu
20 25

(2) INFORMATION FOR SEQ ID NO: 61:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:27

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 61:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Ile Tyr Pro Asn Ala Ser Leu Leu Ile
20 25

(2) INFORMATION FOR SEQ ID NO: 62:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:24

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 62:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Ala Pro Asp Thr Arg Pro Ala Pro
20

(2) INFORMATION FOR SEQ ID NO: 63:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:25

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 63:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Ser Thr Ala Pro Pro Ala His Gly Val
20 25

(2) INFORMATION FOR SEQ ID NO: 64:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:36

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 64:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala
20 25 30

Pro Pro Ala His
35

(2) INFORMATION FOR SEQ ID NO: 65:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:25

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 65:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Tyr Leu Ser Gly Ala Asn Leu Asn Leu
20 25

(2) INFORMATION FOR SEQ ID NO: 66:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:24

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 66:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Glu Ala Gln Asn Thr Thr Tyr Leu
20

(2) INFORMATION FOR SEQ ID NO: 67:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:26

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 67:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Gln Tyr Ser Trp Val Val Asn Gly Thr Phe
20 25

(2) INFORMATION FOR SEQ ID NO: 68:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:25

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 68:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Thr Tyr Ala Cys Phe Val Ser Asn Leu
20 25

(2) INFORMATION FOR SEQ ID NO: 69:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:25

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 69:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Ile Tyr Pro Asn Ala Ser Leu Leu Ile
20 25

(2) INFORMATION FOR SEQ ID NO: 70:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:40

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 70:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Lys Tyr Ala Leu Ala Asp Ala Ser Leu Lys Met Ala Asp Pro
20 25 30

Asn Arg Phe Arg Gly Lys Asp Leu Pro
35 40

(2) INFORMATION FOR SEQ ID NO: 71:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:38

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 71:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Lys Tyr Leu Ala Asp Ala Ser Leu Lys Met Ala Asp Pro Asn Arg Phe
20 25 30

Arg Gly Lys Asp Leu Pro
35

(2) INFORMATION FOR SEQ ID NO: 72:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:34

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 72:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Ser Leu Lys Met Ala Asp Pro Asn Arg Phe Arg Gly Lys Asp
20 25 30

Leu Pro

(2) INFORMATION FOR SEQ ID NO: 73:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:32

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 73:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Ser Leu Lys Met Ala Asp Pro Asn Arg Phe Arg Gly Lys Asp Leu Pro
20 25 30

(2) INFORMATION FOR SEQ ID NO: 74:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:53

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 74:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Leu Tyr Arg Thr Phe Ala Gly Asn Pro Arg Ala Gly Gly Gly Lys Tyr
20 25 30

Ala Leu Ala Asp Ala Ser Leu Lys Met Ala Asp Pro Asn Arg Phe Arg
35 40 45

Gly Lys Asp Leu Pro
50

(2) INFORMATION FOR SEQ ID NO: 75:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:38

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 75:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Gly Val Glu Gly Gly Gly
5 10 15

Glu Arg Ile Lys Thr Thr Ser Ser Ile Glu Phe Ala Arg Leu Gln Phe
20 25 30

Thr Thr Asp His Ile Gln
35

(2) INFORMATION FOR SEQ ID NO: 76:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:40

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 76:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Glu Arg Ile Lys Thr Thr Ser Ser Ile Glu Phe Ala Arg Leu
20 25 30

Gln Phe Thr Thr Asp His Ile Gln
35 40

(2) INFORMATION FOR SEQ ID NO: 77:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:44

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 77:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Ala Thr Leu Tyr Ser Val His Gln Arg Ile Asp Val Lys Asp Thr Lys
20 25 30

Glu Ala Leu Glu Lys Ile Glu Glu Gln Asn Lys Ser
35 40

(2) INFORMATION FOR SEQ ID NO: 78:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:49

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 78:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Ser Gly Gly Gly Ala Thr Leu Tyr Ser Val His Gln Arg Ile Asp Val
20 25 30

Lys Asp Thr Lys Glu Ala Leu Glu Lys Ile Glu Glu Glu Gln Asn Lys Ser
35 40 45

(2) INFORMATION FOR SEQ ID NO: 79:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:57

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 79:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Thr Leu Tyr
20 25 30

Ser Val His Gln Arg Ile Asp Val Lys Asp Thr Lys Glu Ala Leu Glu
35 40 45

Lys Ile Glu Glu Glu Gln Asn Lys Ser
50 55

(2) INFORMATION FOR SEQ ID NO: 80:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:48

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 80:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Gly Ser Ser Ala Thr Leu Tyr Ser Val His Gln Arg Ile Asp Val Lys
20 25 30

Asp Thr Lys Glu Ala Leu Glu Lys Ile Glu Glu Glu Gln Asn Lys Ser
35 40 45

(2) INFORMATION FOR SEQ ID NO: 81:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:47

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 81

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Ala Thr Leu Tyr Ser Val His Gln Arg Ile Asp Val Lys Asp
20 25 30

Thr Lys Glu Ala Leu Glu Lys Ile Glu Glu Glu Gln Asn Lys Ser
35 40 45

(2) INFORMATION FOR SEQ ID NO: 82:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:52

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 82:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Ser Gly Gly Gly Ser Ala Thr Leu Tyr Ser Val His Gln Arg
20 25 30

Ile Asp Val Lys Asp Thr Lys Glu Ala Leu Glu Lys Ile Glu Glu Glu
35 40 45

Gln Asn Lys Ser
50

(2) INFORMATION FOR SEQ ID NO: 83:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:59

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 83:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Thr
20 25 30

Leu Tyr Ser Val His Gln Arg Ile Asp Val Lys Asp Thr Lys Glu Ala
35 40 45

Leu Glu Lys Ile Glu Glu Glu Gln Asn Lys Ser
50 55

(2) INFORMATION FOR SEQ ID NO: 84:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:50

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 84:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Gly Ser Ser Ala Thr Leu Tyr Ser Val His Gln Arg Ile Asp
20 25 30

Val Lys Asp Thr Lys Glu Ala Leu Glu Lys Ile Glu Glu Glu Gln Asn
35 40 45

Lys Ser
50

(2) INFORMATION FOR SEQ ID NO: 85:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:51

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 85:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Ser Leu Tyr Asn Thr Val Ala Thr Leu Tyr Ser Val His Gln Arg Ile
20 25 30

Asp Val Lys Asp Thr Lys Glu Ala Leu Glu Lys Ile Glu Glu Glu Gln
35 40 45

Asn Lys Ser
50

(2) INFORMATION FOR SEQ ID NO: 86:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:56

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 86:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Ser Gly Gly Gly Ser Ser Leu Tyr Asn Thr Val Ala Thr Leu Tyr Ser
20 25 30

Val His Gln Arg Ile Asp Val Lys Asp Thr Lys Glu Ala Leu Glu Lys
35 40 45

Ile Glu Glu Glu Gln Asn Lys Ser
50 55

(2) INFORMATION FOR SEQ ID NO: 87:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:63

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 87:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Leu Tyr Asn
20 25 30

Thr Val Ala Thr Leu Tyr Ser Val His Gln Arg Ile Asp Val Lys Asp
35 40 45

Thr Lys Glu Ala Leu Glu Lys Ile Glu Glu Glu Gln Asn Lys Ser
50 55 60

(2) INFORMATION FOR SEQ ID NO: 88:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:54

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 88:

Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu Gly Gly Gly
5 10 15

Gly Ser Ser Ser Leu Tyr Asn Thr Val Ala Thr Leu Tyr Ser Val His
20 25 30

Gln Arg Ile Asp Val Lys Asp Thr Lys Glu Ala Leu Glu Lys Ile Glu
35 40 45

Glu Glu Gln Asn Lys Ser
50

(2) INFORMATION FOR SEQ ID NO: 89:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:53

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 89:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Ser Leu Tyr Asn Thr Val Ala Thr Leu Tyr Ser Val His Gln
20 25 30

Arg Ile Asp Val Lys Asp Thr Lys Glu Ala Leu Ala Lys Ile Glu Glu
35 40 45

Glu Gln Asn Lys Ser
50

(2) INFORMATION FOR SEQ ID NO: 90:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:58

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 90:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Ser Gly Gly Gly Ser Ser Leu Tyr Asn Thr Val Ala Thr Leu
20 25 30

Tyr Ser Val His Gln Arg Ile Asp Val Lys Asp Thr Lys Glu Ala Leu
35 40 45

Glu Lys Ile Glu Glu Glu Gln Asn Lys Ser
50 55

(2) INFORMATION FOR SEQ ID NO: 91:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:65

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 91:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Leu
20 25 30

Tyr Asn Thr Val Ala Thr Leu Tyr Ser Val His Gln Arg Ile Asp Val
35 40 45

Lys Asp Thr Lys Glu Ala Leu Glu Lys Ile Glu Glu Glu Gln Asn Lys
50 55 60

Ser
65

(2) INFORMATION FOR SEQ ID NO: 92:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:56

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:internal

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 92:

Asp Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu Ile Gly
5 10 15

Gly Gly Gly Ser Ser Ser Leu Tyr Asn Thr Val Ala Thr Leu Tyr Ser
20 25 30

Val His Gln Arg Ile Asp Val Lys Asp Thr Lys Glu Ala Leu Glu Lys
35 40 45

Ile Glu Glu Glu Gln Asn Lys Ser
50 55

(2) INFORMATION FOR SEQ ID NO: 93:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:8

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 93:

Gly Gly Gly Ser Gly Gly Gly Ser
5

(2) INFORMATION FOR SEQ ID NO: 94:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:15

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 94:

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser

5 10 15

(2) INFORMATION FOR SEQ ID NO: 95:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:8

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 95:

Gly Gly Gly Ser Gly Gly Ser Ser

5

(2) INFORMATION FOR SEQ ID NO: 96:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:10

(B) TYPE:amino acid

(C) TOPOLOGY:linear

(ii) MOLECULE TYPE:

(A) DESCRIPTION:peptide

(v) FRAGMENT TYPE:

(ix) FEATURE:

(A) NAME/KEY:

(B) LOCATION:

(C) IDENTIFICATION METHOD:

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 96:

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser

5 10

DECLARATION OF NON-ESTABLISHMENT OF INTERNATIONAL SEARCH REPORT

(PCT Article 17(2)(a), Rules 13*ter* and 39)

Applicant's or agent's file reference CS-112/PCT	IMPORTANT DECLARATION	Date of mailing *(day/month/year)* 27 AUG 2001
International application No. PCT/US01/16793	International filing date *(day/month/year)* 24 MAY 2001	(Earliest) Priority Date *(day/month/year)* 24 MAY 2000
International Patent Classification (IPC) or both national classification and IPC Please See Continuation Sheet.		
Applicant CEL-SCI CORPORATION		

This International Searching Authority hereby declares, according to Article 17(2)(a), that no international search report will be established on the international application for the reasons indicated below.

1. ☐ The subject matter of the international application relates to:
   - a. ☐ scientific theories.
   - b. ☐ mathematical theories.
   - c. ☐ plant varieties.
   - d. ☐ animal varieties.
   - e. ☐ essentially biological processes for the production of plants and animals, other than microbiological processes and the products of such processes.
   - f. ☐ schemes, rules or methods of doing business.
   - g. ☐ schemes, rules or methods of performing purely mental acts.
   - h. ☐ schemes, rules or methods of playing games.
   - i. ☐ methods for treatment of the human body by surgery or therapy.
   - j. ☐ methods for treatment of the animal body by surgery or therapy.
   - k. ☐ diagnostic methods practiced on the human or animal body.
   - l. ☐ mere presentations of information.
   - m. ☐ computer programs for which this International Searching Authority is not equipped to search prior art.

2. ☐ The failure of the following parts of the international application to comply with prescribed requirements prevents a meaningful search from being carried out:
   ☐ the description ☐ the claims ☐ the drawings

3. ☒ The failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions prevents a meaningful search from being carried out.
   - ☐ the written form has not been furnished or does not comply with the standard.
   - ☒ the computer readable form has not been furnished or does not comply with the standard.

4. Further comments:

Name and mailing address of the ISA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	JEFFREY STUCKER
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

Form PCT/ISA/203 (July 1998)*

DECLARATION OF NON-ESTABLISHMENT OF INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/16793

The International Patent Classification (IPC) or National Classification and IPC are as listed below:

IPC(7): A01N 37/18; A61K 38/00, 38/04, 39/21, 39/38; C07K 5/00
US Cl.: 530/324, 326, 328, 329; 424/184.1, 185.1, 188.1, 208.1; 514/2